AMENDMENTS TO THE SPECIFICATION

Please amendment the following paragraphs in the published application 2002/0001853 A1 as follows.

In paragraph [0010]

ok to Enter 11/06

[0010] The binding assay ~~for~~ detects analyte mass rather than analyte concentration, in a liquid sample. An array of sorbent zones is immobilized on a substrate. The sorbent zones include an analyte binding partner, which can be an oligonucleotide probe, antibody, or receptor molecule. When a defined volume of sample, believed to contain an analyte, is deposited on a sorbent zone, the analyte is substantially depleted from the sample to form an analyte capture complex with the analyte binding partner. Analytes of interest can include polynucleotide molecules, antigens, haptens, drugs, and hormones. Generally, the analyte binding partner is present in molar excess relative to the analyte.

In paragraph [0031]

[0031] Reduction of size offers many anticipated advantages to analytical methods, such as reduced costs, faster chemistry, and equivalent or improved sensitivity. The present invention is directed to ligand binding assays in which the analyte is quantified, directly or indirectly, on the basis of its specific affinity for a chemically modified solid material. This broad class includes hybridization assays for specific DNA sequences, ~~immunoassay~~ immunoassays employing immobilized antigen or antibody, and the receptor assays used in high throughput screening of pharmaceuticals. In addition to the benefits noted above, the present invention provides a multianalyte capability with all analytes exposed to the solid phase simultaneously and measured simultaneously.

In paragraph [0037]

[0037] The binding assay of the present inventions can be adapted for use with a variety of liquid samples. Clinical samples, such as blood, serum, plasma, cerebrospinal fluid, or urine, are preferred. An analyte of interest that may be detected in the sample, is preferably a clinically relevant biomolecule capable of binding specifically with a binding partner, such as an oligonucleotide, antibody, or receptor molecule. Such analytes can include antigens, haptens, drugs, hormones and polynucleotides having ~~a~~ specific nucleotide sequences that ~~is~~ are complementary to ~~an~~ particular oligonucleotide probes, antigens, haptens, drugs, and hormones. In preferred versions of the present invention, the analyte is an antigenic substance capable of binding specifically with a capture antibody.

In paragraph [0041]

[0041] In a preferred version of the present invention the sorbent zone includes a first binding partner and a conjugate. The first binding partner can be any of the binding partners listed above, but is most preferably avidin or streptavidin due to the high affinity binding (about 10^{15} liters/mole) of these sorbent materials with biotin. The conjugate is composed of a first ligand and an analyte binding partner. The first ligand can be any of the ligands listed above, depending on the first binding partner, but is most preferably biotin. Accordingly, a most preferred conjugate is a biotinylated antibody.

In paragraph [0044]

[0044] Arrays ~~of~~ can consist of sorbent[[s]] zones of any number, pattern, design, or geometry, e.g., circles, lines, or an $n_{\times}n$ number of spots. Preferably, arrays are an n.times.m matrix of sorbent zones, wherein n is the number of columns and m is the number of rows. The total number of columns and rows can be adapted as needed to a particular application. Adequate spacing between the sorbent zones is desirable to prevent cross contamination by assay reagents and to facilitate

accurate image detection. In a preferred version of the present invention the sorbent zones are aligned in a matrix, wherein the vertical and/or horizontal space between sorbent zones is about 500 μm.

In paragraph [0045]

[0045] Multianalyte binding assays can be conducted by constructing an array having a plurality of sorbent zones, wherein the sorbent zones are divided into subsets of sorbent zones. Each subset of sorbent zones can have ~~a~~ different analyte binding partners immobilized within the sorbent zones of the subset. The subsets may contain identical sorbent zones for the purpose of determining mean values and sampling error. Alternatively, subsets having identical sorbent zones can be used to provide a dose response curve for a particular analyte. Different subsets of sorbent zones having different analyte binding partners can be used to detect and quantify different analytes from the same sample. A preferred version of a multianalyte binding assay, which utilizes an array having subsets of sorbents zones is described in Example III of the present application. In the Example, there are four subsets of sorbent zones. Each subset has five identical sorbent zones, which carry the same monoclonal antibody to a single IgG subtype. Moreover, each subset of five identical sorbent zones utilizes a different monoclonal antibody, each monoclonal antibody recognizing one of four different IgG subtypes.

In paragraph [0066]

[0066] Arrays of immobilized avidin spots were prepared by printing a solution of 1 mg/ml NeutrAvidin in buffered solution. This concentration is higher than typically used for the coating of mictotiter plate wells, but is understandable on the basis of the very different volume-to-surface-area characteristics presented by the microscopic experimental scale. The printed spots dry within 30 seconds of deposition, leaving a visible solid residue which permits visible examination of the

array and gross verification of printer function. For non-covalent immobilization, a 50 mM carbonate buffer at pH 8.2 was used for printing. For covalent immobilization, the buffer was 50 mM phosphate buffered saline at pH 7.4. Covalent immobilization was achieved by derivatization of NeutrAvidin with a commercial photolabile linker moiety. Following printing of this NeutrAvidin-linker conjugate, covalent immobilization was obtained by exposing the dry printed arrays to light from a UV source (Dymax 2000EC, Torrington, Conn.) for three minutes. Subsequent experience with dry avidin arrays has indicated that these materials are stable under refrigerated vacuum ~~dessication~~ desiccation for at least six months.

In paragraph [0078]

[0078] Evidence for subclass specificity is seen in the poor correlations observed if data from a micro-array column is plotted versus myeloma concentrations for the incorrect subclass. Multilinear regression on the multianalyte array data indicates that any cross reactivity between the assays is sufficiently small as to be obscured by the spot-to-spot variability within the columns. This error is currently 10 to 15% of the mean intensity in one column (one standard deviation) owing to mechanical difficulties encountered in the jet printing of multiple analytes. The low level of cross reactivity indicates that antibody specificity can be retained despite the rigors of jet printing and drying. Stability of dry printed multianalyte arrays has been shown to be dependent on the particular antibodies immobilized, but has been demonstrated to exceed one month if arrays are stored in a refrigerated vacuum ~~dessicator~~ desiccator and coated with a commercial immunoassay stabilizer preparation (StableCoat, SurModics Inc., Eden Prairie, Minn.).